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Anal Cancer Screening - A Review

Abstract

Anal cancer rates are rising with increased HPV exposure and HIV prevalence. Similar to cervical cancer, anal cancer is preceded by abnormal epithelial cell changes. These changes can be identified and treated with easy, inexpensive screening tests for individuals at risk of progression to anal cancer.

Keywords: Anal cancer; HPV; AIN; HGAIN; LGAIN; High Resolution Anoscopy; Anal Cytometry

Mini Review

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Abbreviations

HPV: Human Papillomavirus; HIV: Human Immunodeficiency Virus; MSM: Men Who Have Sex With Men; AIN:Anal Intraepithelial Neoplasia; HGAIN: High-Grade Anal Intraepithelial Neoplasia; LGAIN: Low-Grade Anal Intraepithelial Neoplasia; HRA: High Resolution Anoscopy

Mini Review

Though a relatively rare malignancy, the incidence of anal cancer has been steadily rising for decades with 7,270 estimated cases in the United States diagnosed in 2015 [1]. The majority of these cancers are squamous cell carcinomas (85%) [2]. The increase in rates have been attributed to changing sexual practices with increased HPV exposure, as well more individuals living with Immunosuppression and HIV.[1]HIV-infected MSM are an especially high-risk group with incidence rates 60-160 times greater than general population [3]. Though not yet proven, it is expected that screening high-risk groups will allow for earlier identification and treatment of AIN and anal cancer. Similarto early detection and treatment of cervical cancer, anal cancer screening should be effective at reducing the incidence and mortality [4]. Therefore several organizations and the New York State, Department of Health recommend screening for anal cancer in these high-risk populations [1,2].

The anal transitional zone is the junction of the stratified anal squamous epithelium and the glandular columnar epithelium of the rectum that undergoes metaplasia. These metaplastic cells are most susceptible to transformation by oncogenic HPVs causing anal intraepithelial neoplasia (AIN) [5,6]. AIN precedes anal cancer and has three gradations: AIN 1 is mild; AIN 2 is moderate; AIN 3 is severe. Further terminology has AIN 1 as low-grade AIN (LGAIN) and AIN 2/3 as high-grade AIN (HGAIN). HGAIN is seen in 25-52% of HIV-infected MSM with AIN and progresses to anal cancer in up to 16% of these individuals [7]. As with cervical cancer, anal cancer is preceded by these precursor lesions and early identification, surveillance and treatment can be paramount in decreasing the incidence of anal squamous cell cancer.

Currently there is no standardization for screening, but advocates for ASCC prevention accept anal cytology, combined with high-resolution anoscopy (HRA), as the best test for screening of precancerous lesions [8-10]. Anal cytology is analogous to the cervical Pap smear. The technique is performed by gently inserting a moistened swab into the anal canal until the swab abuts the distal rectal wall, most commonly without direct visualization of the canal. After a full circumferential rotation, the swab is slowly withdrawn with pressure - sampling the entire length of the anal canal [10]. Despite its cost-effectiveness of ~$90/procedure, anal cytology has a wide range and low sensitivity and specificity (42-98% and 33-96%, respectively) for AIN lesions, frequently not recognizing HGAIN [3,11] Due to its inaccuracy, individuals with abnormal cytology should subsequently undergo HRA to identify, biopsy and treat dysplastic lesions [12].

HRA is considered the gold standard for surveillance and detection of recurrent AIN [3,12]. First developed in the early 1990s, HRA utilizes colposcopic visualization of the anal canal and perianus after acetic acid or Lugol's solution application. Precancerous squamous lesions are then visible with magnification, facilitating biopsy and even treatment of the previously small, invisible lesions [13]. Therapies for AIN range from topical treatments, most frequently imiquinod and fluorouracil, to surgical fulguration and/or excision [2]. Several studies have found HRA to be highly sensitive with a lower specificity (59-100% and 19-74%, respectively) for AIN, necessitating biopsy of any unsuspecting atypical lesions [5]. HRA is the most expensive screening procedure ($193/procedure), yet it has been found to be the most cost-effective in high-risk populations and even considered first line HGAIN screening in HIV-infected individuals [3,7].

Prevention against anal cancer is possible with both behaviorial and non-behavioral interventions. Safer sex, such as condom use and limiting the number of sexual partners, decreases HPV-related diseases. Smoking cessation has benefits since anal cancer and cytologic abnormalities are linked to tobacco use. Medication compliance to keep HIV viral loads low and CD4+ counts high adds protection against AIN. Foods high in antioxidants have been shown to reduce progression of HPV to HGAIN. The newest prevention method is the quadrivalent HPV vaccine. It protects against HPV types 6, 11, 16, and 18 and reduced high-grade dysplasia rates by more than 50% in the

treatment population [15]. With further application, anal cancer rates should be reduced.

Even with preventative and screening techniques available, Factor et al. [9]. asked if colon and rectal surgeons were ready to screen for AIN. With a resounding no, the respondents claimed cost, low priority, and a lack of training as major barriers. Lacking evidence was also a major obstacle to screening [9]. Therefore, we anxiously await the results of the large, randomized controlled Anal Cancer/HSIL Outcomes Research (ANCHOR) trial currently being conducted to evaluate the benefits of treating versus close observation without treatment of precancerous anal lesions [1,14].

Conclusion

With increasing anal cancer rates, it is important to identify at-risk individuals. Our current screening methods, which include anal cytometry and HRA, remain the gold standard for identifying AIN. In high-risk groups, such as HIV-infected individuals, direct use of HRA should be considered the first line of surveillance, pending new data from the ANCHOR trial [3].

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